

**Amendment and Response**

Page 2 of 16

Serial No.: 10/732,782

Confirmation No.: 6883

Filed: December 10, 2003

For: CHEMOPREVENTIVE AND THERAPEUTIC ASPECTS OF POLYPHENOLIC COMPOSITIONS AND ASSAYS

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**Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. (withdrawn) A method of determining if cancer cells are resistant to an agent, the method comprising:

determining the p57/KIP2 level in the cancer cells prior to contact with the agent;  
contacting the cancer cells with the agent;  
determining the p57/KIP2 level in the cancer cells after contact with the agent; and  
comparing the p57/KIP2 level in the cancer cells after contact with the agent to the p57/KIP2 level in the cancer cells prior to contact with the agent;

wherein an increase in the p57/KIP2 level in the cancer cells after contact with the agent compared to the p57/KIP2 level in the cancer cells prior to contact with the agent indicates the cancer cells are resistant to the agent.

2. (withdrawn/currently amended) The method of claim [[1]] 10, wherein the cancer cell is an epithelial carcinoma cell line.

3. (withdrawn/currently amended) The method of claim 2, wherein the epithelial carcinoma cell lines line is selected from the group consisting of an oral squamous carcinoma cell line, a metastatic oral carcinoma cell line, and a breast epithelial carcinoma cell line.

4. (withdrawn/currently amended) The method of claim [[1]] 10, wherein the cancer cells are derived from a human epithelial carcinoma.

**Amendment and Response**

Page 3 of 16

Serial No.: 10/732,782

Confirmation No.: 6883

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For: CHEMOPREVENTIVE AND THERAPEUTIC ASPECTS OF POLYPHENOLIC COMPOSITIONS AND ASSAYS

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5. (withdrawn) The method of claim 4, wherein the human epithelial carcinoma is selected from the group consisting of an oral squamous carcinoma, a metastatic oral carcinoma, and a breast epithelial carcinoma.
6. (withdrawn/currently amended) The method of claim [[1]] 10, wherein determining the p57/KIP2 level is by detecting the p57/KIP2 protein.
7. (withdrawn/currently amended) The method of claim [[1]] 10, wherein determining the p57/KIP2 level is by detecting the mRNA encoding p57/KIP2.
8. (withdrawn) A method of determining if cancer cells are sensitive to an agent, the method comprising:
- determining the p57/KIP2 level in the cancer cells prior to contact with the agent;
  - contacting the cancer cells with the agent;
  - determining the p57/KIP2 level in the cancer cells after contact with the agent; and
  - comparing the p57/KIP2 level in the cancer cells after contact with the agent to the p57/KIP2 level in the cancer cells prior to contact with the agent;
- wherein no increase in the p57/KIP2 level in the cancer cells after contact with the agent compared to the p57/KIP2 levels in the cancer cells prior to contact with the agent indicates the cancer cells are sensitive to the agent.
9. (withdrawn) A method of identifying an agent effective for the treatment of a cancer, the method comprising:
- determining the p57/KIP2 level in cancer cells prior to contacting with the agent;
  - contacting the cancer cells with the agent;
  - determining the p57/KIP2 level in the cancer cells after contacting with the agent; and
  - comparing the p57/KIP2 level in the cancer cells after contacting with the agent to the

**Amendment and Response**

Page 4 of 16

Serial No.: 10/732,782

Confirmation No.: 6883

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p57/KIP2 level in the cancer cells prior to contacting with the agent;

wherein no increase in the p57/KIP2 level in the cancer cells after contacting with the agent compared to the p57/KIP2 level in the cancer cells prior to contacting with the agent indicates the agent is effective for the treatment of a cancer.

10. (original) A method of determining the therapeutic effectiveness of an agent, the method comprising:

contacting normal cells with the agent;

determining the p57/KIP2 level in the normal cells after contacting with the agent;

contacting cancer cells with the agent;

determining the p57/KIP2 level in the cancer cells after contacting with the agent; and

comparing the p57/KIP2 level in the normal cells after contacting with the agent to the p57/KIP2 level in the cancer cells after contacting with the agent;

wherein a higher p57/KIP2 level in the normal cells compared to the p57/KIP2 level in the cancer cells indicates the agent is effective for the treatment of cancer.

11. (original) The method of claim 10, wherein the normal cells and cancer cells are cultured together.

12. (withdrawn) A method of optimizing the formulation of an agent for the treatment of a cancer, the method comprising:

contacting cancer cells with a first formulation of the agent;

determining the p57/KIP2 level in the cancer cells contacted with the first formulation of the agent;

contacting cancer cells with a second formulation of the agent;

determining the p57/KIP2 level in the cancer cells contacted with the second formulation of the agent; and

**Amendment and Response**

Page 5 of 16

Serial No.: 10/732,782

Confirmation No.: 6883

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comparing the p57/KIP2 level in the cancer cells contacted with the first formulation of the agent to the p57/KIP2 level in the cancer cells contacted with the second formulation of the agent;

wherein the formulation with the lower level of p57/KIP2 indicates the formulation of the agent more effective for the treatment of a cancer.

13-16. (cancel)

17. (withdrawn/currently amended) The method of claim [[13]] 10, wherein the cancer cells are selected from the group consisting of oral cancer, esophageal cancer, gastric cancer, colorectal cancer, prostate cancer, bladder cancer, skin cancer, and cervical cancer.

18-24. (cancel)

25. (withdrawn/ currently amended) The method of claim [[24]] 10, wherein both the tumor cancer cells and normal cells are of epithelial origin.

26. (withdrawn/currently amended) The method of claim [[24]] 10, wherein both the tumor cancer cells and normal cells are human cells.

27-32. (cancel)

33. (withdrawn/currently amended) The method of claim [[30]] 10, wherein the normal cells are normal human primary epidermal keratinocytes or fibroblasts.

34-35. (cancel)